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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/519,342	09/21/2005	Dean Y Li	UUTH-P01-010	2504

7590
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06/24/2009

EXAMINER

ROMEO, DAVID S

ART UNIT

PAPER NUMBER

1647

MAIL DATE

DELIVERY MODE

06/24/2009

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/519,342	LI ET AL.	
	Examiner	Art Unit	
	David S. Romeo	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 19 May 2009.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 7-9 and 19-21 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 7-9 and 19-21 is/are rejected.
- 7) ☒ Claim(s) 7 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>0509</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is
5 eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 05/19/2009 has been entered.

Claims 7–9 and 19–21 are pending and being examined.

Maintained formal matters, objections, and/or rejections:

10 ***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

15 The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 7–9 and 19–21 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of inhibiting the migration of HMVECs *in vitro* using Slit2 ligand, does not reasonably provide enablement for a method of inhibiting the
20 migration of HMVECs without regard to the system in which the Slit ligand is employed or for a method of preventing angiogenesis. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The one working example in the specification is limited to disclosing that Slit2 inhibits
25 the migration of HMVECs expressing Robo4 (paragraph [0045]) in an *in vitro* cell migration

Art Unit: 1647

assay (Figure 7). The claims are directed to or encompass a method of inhibiting the migration of HMVECs and/or preventing angiogenesis whenever and wherever angiogenesis is occurring by activating a Robo4 receptor with any Slit ligand or Slit2. Dr. Li acknowledges that “Migration of endothelial cells and formation and migration of endothelial tubes are essential in the process of angiogenesis.” See the declaration filed 10/29/2008, paragraph 15.

The rejection of record cited references that found results counter those disclosed and claimed in the present application, and held that there is a lack of predictability in the art, angiogenesis and vascular guidance are complex, and the working examples and guidance in the specification are limited. Furthermore, Wang (Cancer Cell. 2003 Jul;4(1):19-29) indicates that Slit2 increases microvessel densities *in vivo* (paragraph bridging pages 21-22 through page 22, paragraph bridging left and right columns). Wang (Cancer Sci. 2008 Mar;99(3):510-7) teaches that increased Slit2 expression was associated with higher tumor angiogenesis, as reflected by increased microvessel density (Abstract). These results indicate that Slit2 promotes angiogenesis and microvessel migration.

Okada (Circ Res. 2007 Jun 22;100(12):1712-22) coupled a 3-kb human Robo4 promoter to LacZ, and the resulting cassette was introduced into the Hprt locus of mice by homologous recombination. Reporter gene activity was observed in the vasculature of adult organs (particularly in microvessels). See the Abstract. Tissue sections revealed LacZ staining in the endothelial lining of vessels in all organs examined (Figure 7B). Expression was greater in the microvessels compared with macrovessels. See page 1719, left column, last full paragraph. Okada’s results indicate that microvascular endothelial cells express a native Robo-4 receptor,

Art Unit: 1647

and that Wang's results, above, that are opposite to those claimed are not due to a lack of Robo-4 expression in Wang's experimental system.

For the specification to enable the skill artisan to make and use the claimed method it is incumbent upon applicant to set forth the procedures to achieve the desired results. Otherwise, the claims are an invitation to experiment. In view of the contravening evidence, the lack of predictability in the art, the complexity in the art, the limited working examples and guidance provided by the specification and the breadth of the claims, the examiner concludes that it would require undue experimentation for the skilled artisan to use the full scope of the claimed invention.

Response to Arguments

Applicant's arguments filed 05/19/2009 have been fully considered but they are not persuasive.

Applicants argue that the Examiner has acknowledged that the specification is "enabling for a method of inhibiting migration of HMVECs." However, at the time it was the examiner's understanding that the inhibition of HMVEC migration was an *in vitro* system for monitoring angiogenesis. It is now clear that the claims encompass both *in vitro* and *in vivo* methods. The specification has not enabled *in vivo* methods of inhibiting HMVEC migration, as discussed above.

New Formal Matters, Objections and/or Rejections

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Art Unit: 1647

Claims 19–21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 19 is indefinite because it lacks a process step which clearly relates back to the claim preamble and it is unclear whether preventing angiogenesis is achieved; an intended use is not the same as achieving a result; it is unclear what result of the process can be inferred. Claims 20 and 21 depend from claim 19, and thus share this defect with claim 19. The metes and bounds are not clearly set forth.

Claim Objections

Claim 7 is objected to because of the following informalities: the phrase “inhibiting migration human” appears to be grammatically incorrect. It is suggested that the claim recite “inhibiting the migration of human.”. Appropriate correction is required.

Conclusion

No claims are allowable.

ANY INQUIRY CONCERNING THIS COMMUNICATION OR EARLIER COMMUNICATIONS FROM THE EXAMINER SHOULD BE DIRECTED TO DAVID S. ROMEO WHOSE TELEPHONE NUMBER IS (571) 272-0890. THE EXAMINER CAN NORMALLY BE REACHED ON MONDAY THROUGH FRIDAY FROM 9:00 A.M. TO 5:30 P.M. IF ATTEMPTS TO REACH THE EXAMINER BY TELEPHONE ARE UNSUCCESSFUL, THE EXAMINER'S SUPERVISOR, MANJUNATH RAO, CAN BE REACHED AT (571)272-0939.

IF SUBMITTING OFFICIAL CORRESPONDENCE BY FAX, APPLICANTS ARE ENCOURAGED TO SUBMIT OFFICIAL CORRESPONDENCE TO THE CENTRAL FAX NUMBER FOR OFFICIAL CORRESPONDENCE, WHICH IS (571) 273-8300.

CUSTOMERS ARE ALSO ADVISED TO USE CERTIFICATE OF FACSIMILE PROCEDURES WHEN SUBMITTING A REPLY TO A NON-FINAL OR FINAL OFFICE ACTION BY FACSIMILE (SEE 37 CFR 1.6 AND 1.8).

ANY INQUIRY OF A GENERAL NATURE OR RELATING TO THE STATUS OF THIS APPLICATION OR PROCEEDING MAY BE OBTAINED FROM THE PATENT APPLICATION INFORMATION RETRIEVAL (PAIR) SYSTEM. STATUS INFORMATION FOR PUBLISHED APPLICATIONS MAY BE OBTAINED FROM EITHER PRIVATE PAIR OR PUBLIC PAIR. STATUS INFORMATION FOR UNPUBLISHED APPLICATIONS IS AVAILABLE THROUGH PRIVATE PAIR ONLY. FOR MORE INFORMATION ABOUT THE PAIR SYSTEM, SEE [HTTP://PAIR-DIRECT.USPTO.GOV](http://PAIR-DIRECT.USPTO.GOV). CONTACT THE ELECTRONIC BUSINESS CENTER (EBC) AT 866-217-9197 (TOLL-FREE) FOR QUESTIONS ON ACCESS TO THE PRIVATE PAIR SYSTEM,

/DAVID S ROMEO/
PRIMARY EXAMINER, ART UNIT 1647